REMARKS/ARGUMENTS

Claims 1-7, 11-21, and 23-28 have been cancelled. Claims 8, 9, and 22 have been amended. Claims 29-32 have been added. Support for amended claims 8, 22, and added claims 29-32 can be found in the specification and claims as filed, for example claims 1-6. Support for amended claims 8 and 22 can be found in the specification as filed, for example ¶51. Claim 9 was amended to correct a minor informality. No amendment should be construed as an acquiescence in any ground of rejection. No new matter has been added herewith.

The specification has been amended to remove an embedded hyperlink.

Rejection under 35 U.S.C.§112, second paragraph

Claims 1-10 were rejected as indefinite for the following reasons.

The office action stated that the recitation of the following language in claims 1 and 4 was indefinite, "the BLASTP algorithm with a word length and the BLOSUM62 scoring matrix." The office action states that this is "because the algorithm may vary with different release versions and a number of versions have been released." Claims 1-4 have been cancelled, but, the language has been maintained in amended claims 8 and 22. Applicants respectfully disagree with the rejection.

The BLAST algorithms have been provided in the claims as a method to determine sequence identity. BLAST is a program that uses a standard method of identifying identity between two sequences. BLAST has been used in many allowed claims to set forth the metes and bounds of sequence identity (three exemplary patents are provided in Appendix A). The Examiner refers to the fact that there are various release versions of the BLAST algorithm. However, Applicants have provided clear information in the specification (including citations) as to how the BLAST algorithm works and the parameters of the specific search. For this reason, the release version of the BLAST algorithm is not necessary for one of skill to determine the metes and bounds of the claims. A detailed recitation of the way BLAST functions is provided as well as the specific algorithm used in the methods herein, in the specification on page 7, ¶s 25 and 26. Further, three references are cited to provide further information about performing the

algorithm (see Altschul *et al.* 3rd line of ¶25; Henikoff & Henikoff, last line of ¶25; and Karlin & Altschul, 3rd line of ¶26). With this information the skilled artisan would be able to ascertain how to use the algorithm for sequence identity calculations with or without the same release version of the program. Therefore, the reference to the BLAST program is believed definite.

The recitation of "the polynucleotide sequence" in claim 6, "the transporter" in claim 9, and "the cell" in claim 10 were rejected as indefinite for insufficient antecedent basis. The claims have been amended as follows, claim 6 has been cancelled, rendering the rejection moot. Claim 9 has been amended to be dependent upon claim 8 which provides antecedent basis for "the transporter" and "the cell." As a result of the amendments, Applicants respectfully request withdrawal of the rejections.

Rejection under 35 U.S.C.§112, first paragraph, written description

Claims 1, 3-5 and 7-8 were rejected as allegedly failing to comply with the written description requirement for all variants of SEQ ID NO:1 and 2 as claimed. The Office Action states that "in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus." The specification fails to describe any characteristic or structure of a genus "a polypeptide having 80% sequence identity to the SEQ ID NO:2" or "a nucleic acid having 80% sequence identity to the SEQ ID NO:1."

As discussed in the MPEP, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice...or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Applicants have provided a description of the relevant identifying characteristics of the class of transporters exemplified by SEQ ID NO:2 by disclosure of the structures and the

functional limitations that have been added to the claims. The structures and properties of transporters are well known in the art and are discussed in ¶2 of the specification as having "a plurality of membrane-spanning loops." The transporter of SEQ ID NO:2 is a solute carrier-mediated transporter having homology to the Ostα and β transporters identified in Wang et al. (see specification ¶5). These transporters have certain known structural features, such as the helical transmembrane domains, the glycosylation sites, and the cysteine residues in the fourth hydrophilic domain (see ¶47 and 48 of the specification). Using this information, the skilled artisan could design variants that retain these features. More obvious variants are discussed in ¶30-32, such as allelic variants, conservative modifications, and silent variants.

Applicants have further amended the claims to include a functional limitation for the variants, namely that they have "the transporter activity of the transporter encoded by SEQ ID NO:1" or the equivalent language with respect to the protein sequence. Thus, the variants and fragments used in the screening method in addition to having the specified sequence identity also have the transporter activity of SEQ ID NO:2 (hOCT4), for example they transport the substrate taurocholate (see ¶10). Methods of identifying variants are discussed in the specification in ¶50-53. Methods of identifying whether the variants have the activity of the transporter of SEQ ID NO:2 are provided in ¶67.

This information in combination with the knowledge of the skilled artisan provides sufficient written description for the genus of "a polypeptide having 80% sequence identity to the SEQ ID NO:2" or "a nucleic acid having 80% sequence identity to the SEQ ID NO:1."

The PTO's Guidelines for application of the written description requirement explicitly recognizes that a class of proteins can be defined in functional terms without providing sequence data. That is, for example, for the class of proteins antibodies, a claim to "[a]n isolated antibody capable of binding to antigen X," meets the guidelines notwithstanding lack of any sequence data for the antibody. The functional definition of an antibody is sufficient because of "the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of

antibody binding, and the fact that the antibody technology is well developed and mature." *See* Example 6 of the Synopsis of Application of Written Description Guidelines.

The cases cited by the Examiner are distinguished from the present facts. The *Vas-Cath* case arose in the typical context of determining new matter. Specifically, the issue was whether drawings of a catheter in a design application provided written description of claims that appeared in a utility application claiming priority to the design application. However, here the Examiner's rejection is applied to originally filed claims and no issue of new matter has been raised.[1] *Vas-Cath* does not address what written description is required for originally filed claims.

The Fiers, Amgen, and Fiddes cases address written description in situations in which the invention lies in cloning a nucleic acid encoding a particular protein, such as human EPO or FGF for the first time. In circumstances in which the invention lies in cloning a gene, it is perhaps not unreasonable that a newly isolated gene cannot be described without determining its sequence. By contrast, in the present claims, the invention lies not in the de novo isolation of a new gene, such as the gene encoding EPO, but rather in the use of nucleic acids encoding a transporter that has a known activity and substrate for a particular purpose (*i.e.*, identifying other substrates for the transporter). In such an invention, it is submitted that written description is provided by the recital of the known function of the transporter (transporting a substrate through a plasma membrane), the well known conserved features of transporters (transmembrane domains), and the mature states of the art as provided in the PTO Guidelines.

For these reasons, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C.§112, first paragraph, enablement

Claims 1, 3-5, and 7-8 were rejected as failing to comply with the enablement requirement. The Office Action states that "while being enabling for the polypeptide of SEQ ID NO:2 or the nucleic acid sequence of SEQ ID NO:1, [the specification] does not reasonably

[1] The claims are amended in this amendment. However, the rejection as phrased in the office action was directed to the original claims.

provide enablement for any polypeptide having 80% sequence identity to the SEQ ID NO:2 or any nucleic acid having 80% sequence identity to the polynucleotide of SEQ ID NO:1."

The test for enablement involves identifying whether the experimentation needed to practice the invention is undue or unreasonable (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether any experimentation needed is "undue." These include the breadth of the claims, the state of the prior art, the level of predictability in the art, the amount of direction provided, and the existence of working examples. These are set out below.

The breadth of the claims - The claims set out very specific structural and functional guidelines for what a variant is, specifically, any polypeptide having 80% sequence identity to the SEQ ID NO:2 or any nucleic acid having 80% sequence identity to the polynucleotide of SEQ ID NO:1 and the resulting variant transporter having the transporter activity of the transporter of SEQ ID NO:2.

The state of the prior art - The art of transporters is very old. The structures and properties of transporters have been known in the art for a very long time, particularly the helical transmembrane domains. Allelic and conservative variants of these transporters and fusion proteins that result in the fusion of various portions of one transporter with a second transporter have been generally known or in practice. The use of fusion proteins was used to identify specific domains in transporters, such as the substrate binding and transmembrane domains, for example. Thus, there is a high level of predictability for the ability to make variants of transporters that still have the substrate binding and transporting activity of the original.

The amount of direction provided - With respect to the statement that "the specification does not teach any variant, fragment, or derivative of the polypeptide other than the full-length sequence (including functional or structural characteristics)", Applicants respectfully disagree. As discussed above in the written description rejection, structural characteristics that are to be conserved are taught in ¶s 2, 5, 47 and 48; various types of variants are taught in ¶s 30-32; functional characteristics of the variants are taught in the claim as amended and in ¶51.

Taurocholate or estrone-3-sulfate transport can be used as substrates in screening assays to identify structural activity of transporter variants ¶69, ¶s 65-70.

Using this information and the knowledge of the skilled artisan, it would not require undue experimentation to identify or to produce variants having the specified identity and function and Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C.§102(e)

Claims 1, 3-5, and 7-8 were rejected as anticipated under 35 U.S.C. §102(e) by Kato et al (USPN 20040034192, priority date of 12/8/2000). Claims 1-7 were cancelled. With respect to anticipation of the subject matter of claim 8, Applicants respectfully disagree.

Amended claim 8 and the remaining claims are specific to screening methods for identifying substrates for the transporter protein SEQ ID NO:2 and variants. The substrates are identified by contacting them with the transport protein and identifying whether they are transported into a cell.

To be anticipatory a reference must disclose each and every element of the claims. Kato is not anticipatory because Kato does not teach a method of screening agents, conjugates, or conjugate moieties for the ability to be transported by the transporters of SEQ ID NO:2 and variants. In the Office Action, the Examiner alleges that SEQ ID NO:38 in Kato is a variant of the sequence of SEQ ID NO:2 and that Kato teaches that the polypeptide of SEQ ID NO:38 is a transporter (specifically in ¶307 of Kato).

Applicants respectfully disagree. Kato does not teach a person of ordinary skill in the art that protein SEQ ID NO:38 is a transport protein. The Examiner is mistaken that ¶307 in Kato teaches that SEQ ID NO:38 is a transport protein. ¶305-307 discuss only SEQ ID NOs: 122, 132, and 142 and only suggests that SEQ ID NOs: 122, 132, and 142 are similar to a mouse cation transport protein. These sequences are not related in any way to SEQ ID NO: 38 in Kato. Further, the paragraph in Kato et al. that does discuss SEQ ID NO:38 (¶223) states only that "The ORF encodes a protein consisting of 340 amino acid residues and there existed six putative transmembrane domains." This suggests only that SEQ ID NO:38 is a membrane protein. It

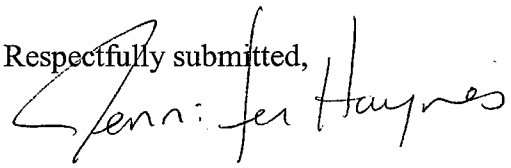
does not suggest that the protein is a transporter. Many membrane proteins having transmembrane domains function other than as transporter proteins. Thus, Kato does not teach all of the elements recited in claim 8 or any of the amended or added claims, and Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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